BMJ Best Practice

Hypoventilation syndromes

Straight to the point of care

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Summary

Hypoventilation syndrome comprises disorders associated with alveolar hypoventilation (an elevation in $PaCO_2$ to levels >45 mmHg). Hypoxemia is also present in most cases, especially during sleep (PaO_2 <60 mmHg).

Alveolar hypoventilation can occur with obesity hypoventilation syndrome, restrictive thoracic disorders, central sleep apnea syndromes, and COPD.

Symptoms are often nonspecific, but almost always include disturbed sleep and impaired daytime function.

Physical exam often reveals signs of cor pulmonale in addition to those associated with the primary disorder.

Diagnosis is usually made by the clinician's awareness that alveolar hypoventilation is often associated with certain medical disorders. Investigations include arterial blood gas analysis, pulmonary function tests, measurement of respiratory muscle strength, and an overnight polysomnogram.

Treatment involves nocturnal ventilation, including the use of invasive ventilation.

Definition

Alveolar hypoventilation, defined as an elevation in $PaCO_2$ to levels >45 mmHg, can occur with several disorders: obesity hypoventilation syndrome, restrictive thoracic disorders, central sleep apnea syndromes, and COPD.[1] These are referred to as the hypoventilation syndromes. Associated with hypercapnia is the development of hypoxemia, which adds to the clinical manifestations and morbidity. In addition, during sleep, hypoventilation becomes more profound and can worsen pre-existing hypercapnia and hypoxemia. In some cases, hypercapnia and hypoxemia may develop only during sleep, which may be unsuspected based on awake values.

Epidemiology

The prevalence of the hypoventilation syndrome varies with the underlying cause. Approximately 10% to 20% of patients with obstructive sleep apnea (OSA) are reported to have obesity hypoventilation syndrome (OHS).[2] [3] [4] However, approximately 10% of patients with OHS have an apnea-hypopnea index that is normal at <5 events/hour.[2] [3] In patients with congestive heart failure and a left ventricular ejection fraction of <45%, Cheyne-Stokes respiration is reported in 33% to 42% of patients, with a prevalence as high as 56% in inpatients awaiting cardiac transplantation.[5] [6] [7] [8] In patients with underlying COPD, approximately 27% developed nocturnal hypoxemia, but only those with associated OSA (referred to as the overlap syndrome) or with severe obstruction (FEV1 <35% predicted) may demonstrate associated hypercapnia. In patients with restrictive thoracic disorders, such as chest wall deformities (e.g., kyphoscoliosis), the prevalence of hypoventilation is dependent on the degree of spinal curvature (Cobb angle >120°), while patients with neuromuscular diseases may all eventually develop hypoventilation syndrome, depending on the underlying disease (e.g., Duchenne muscular dystrophy).

Etiology

Some disease states have been associated with hypoventilation syndromes. These include obesity hypoventilation syndrome and restrictive thoracic disorders, such as in patients with chest wall deformities (e.g., kyphoscoliosis, fibrothorax, or thoracoplasty) and neuromuscular disorders, particularly Duchenne muscular dystrophy and other types of muscular dystrophies and spinal muscular atrophies. Also included are patients with central sleep apnea syndromes, such as idiopathic central sleep apnea, and patients with Cheyne-Stokes respiration. Another central but rare disorder is primary alveolar hypoventilation. Finally, obstructive airway disease (in particular, COPD) can develop alveolar hypoventilation and be included in the hypoventilation syndromes.

Pathophysiology

The mechanisms responsible for the development of hypoventilation include:

- A decrease in central respiratory drive
- Chest wall and lung parenchymal deformities
- Respiratory muscle weakness.

In many disorders that provoke hypoventilation, more than one mechanism is responsible. In addition, in many disorders hypoventilation may first occur during sleep, when hypoxic and hypercapnic ventilatory responses are normally decreased compared with during wakefulness, and REM-sleep-related inhibition of spinal motor neurons can have a major effect.[9] [10] CO_2 retention during sleep will lead to a compensatory retention of bicarbonate by the kidney, which further blunts central drive and promotes more CO_2 retention, contributing to sleep fragmentation with arousals. In patients with obesity-related hypoventilation, a blunted central response, decreases in chest wall and lung parenchymal compliance, presence of obstructive sleep apnea (OSA), and a leptin-resistance state (a satiety protein that increases ventilation) all contribute.[11] [12] [13] [14][15] In patients with neuromuscular disease, hypoventilation, especially during REM sleep, is the result of the loss of accessory muscle contribution to breathing in the setting of a weakened diaphragm, as well as upper airway obstruction resulting in OSA.[16] Similar mechanisms are responsible for the hypoventilation in patients with thoracic cage abnormalities.[17] Hyperventilation-induced hypocapnia, in the presence of an increased central and peripheral responsiveness to CO_2, seems an important mechanism for

the development of Cheyne-Stokes respiration during sleep in patients with congestive heart failure.[18] [19] [20] [21] [22]

Case history

Case history #1

A 52-year-old woman with a history of chronic obesity (BMI = 38 kg/m²) presents with a 2-week history of increasing shortness of breath and lower-extremity swelling. In addition, the patient reports increasing daytime sleepiness and morning headaches. Vital signs are significant for a pulse oximetry reading of 86% on room air. Physical exam reveals a small, crowded oropharynx; an enlarged neck circumference (48 cm); an increased P2 on cardiac auscultation; an enlarged abdomen; and 3+ lower-extremity edema. Basic laboratory investigations are remarkable for an elevated serum bicarbonate of 32 mEq/L. An arterial blood gas is obtained revealing a pH of 7.28, $PaCO_2$ of 68 mmHg, PaO_2 of 56 mmHg, and SaO_2 of 85%.

Other presentations

In many of the underlying conditions that make up the hypoventilation syndromes, patients may present initially with complaints associated with disturbed sleep, including frequent nocturnal awakenings, nonrestorative sleep, loud snoring, and witnessed apneas. In addition, in those patients with conditions associated with respiratory muscle weakness, impaired cough and repeated lower respiratory tract infections may also complicate the patient's course of illness. Finally, some patients may present in overt respiratory failure requiring emergent ventilatory support.

Approach

Clinical suspicion is central to diagnosing hypoventilation syndromes. Many of these disorders commonly present with, or develop, alveolar hypoventilation. It is with this knowledge that clinicians should first question and then confirm whether the patient's signs and symptoms can be explained by the diagnosis of alveolar hypoventilation.

Disease states that have been associated with the hypoventilation syndromes include:[1]

- Obesity hypoventilation syndrome (OHS)
- Restrictive thoracic disorders, such as patients with chest wall deformities (e.g., kyphoscoliosis, fibrothorax, or thoracoplasty)
- Neuromuscular disorders, particularly Duchenne muscular dystrophy and other types of muscular dystrophies and spinal muscular atrophies
- Central sleep apnea syndromes, such as idiopathic central sleep apnea, and Cheyne-Stokes respiration (CSR)
- Congenital central alveolar hypoventilation, which is a rare disorder
- Obstructive airway disease (in particular, COPD).

This topic focuses on OHS, restrictive thoracic disorders, Cheyne-Stokes respiration, and COPD.

See Central sleep apnea , Obstructive sleep apnea , and Muscular dystrophies .

History

Many of the symptoms secondary to the disorder causing hypoventilation are nonspecific and of limited value. In the early stages of the disorder, the patient may be totally asymptomatic. However, as the syndrome progresses, dyspnea on exertion followed by dyspnea at rest is the most common symptom encountered by patients with hypoventilation. Disturbed sleep and daytime hypersomnolence resulting from nocturnal hypoventilation may progress and be associated with symptoms of morning headaches and fatigue. If a disorder causes respiratory muscle weakness, impaired cough and repeated lower respiratory tract infections may also complicate the patient's course. In addition, careful history-taking can allow one to determine the rate of progression of the underlying disorder, in order to initiate appropriate therapeutic interventions.

Congenital central alveolar hypoventilation typically presents in newborns, with symptomatic and asymptomatic children surviving to adulthood.[25] [26] [27] In patients with neuromuscular disease, sleep-disordered breathing, including nocturnal alveolar hypoventilation, presents in childhood.[16] [28] Patients with obesity hypoventilation are usually middle-aged.[23] Patients with COPD and those with CSR are usually in the age range of 40 to 60 years, but this can be variable. In patients with OHS, there is a 2:1 male-to-female ratio.[23]

Physical examination

The value of the physical exam is not only in characterizing the cause of hypoventilation (e.g., chest wall deformity, obesity [BMI ≥30 kg/m²], severe COPD) but also in detailing the severity of the complications that result from it (e.g., the presence of cor pulmonale). While a precipitating event such as a respiratory tract infection can trigger acute respiratory failure at any time, most patients' physical exam reflects the more usual, gradual progressive development of alveolar hypoventilation over months or years. As a result of diurnal CO_2 retention and associated hypoxemia, patients may demonstrate signs of cor

pulmonale, including an increased pulmonic component of the second heart sound (P2), and lower-extremity edema. An increased P2 can be seen with most causes of hypoventilation syndrome.[16] [23] [28] Patients with OHS have a BMI ≥30 kg/m², with an increasing prevalence with increasing BMI.[23] Lower-extremity edema and right-sided third heart sound (S3 gallop) are evident with most causes of hypoventilation syndrome.[16] [23] [28]

Other conditions, such as CSR, may present with physical findings suggestive of left-sided congestive heart failure (CHF), such as an S3 gallop, and inspiratory crackles on examination of the lungs. A left-sided fourth heart sound (S4 gallop) can be seen in patients with CSR due to CHF.

Confirmatory investigations

An arterial blood gas analysis is required in all patients to document the presence of an elevated CO_2 and confirm the diagnosis. It is the definitive test used to confirm the diagnosis of alveolar hypoventilation and to document the extent of associated hypoxemia.[29] If hypoventilation becomes more severe, hypercapnia or hypoxemia becomes more evident, and respiratory failure may ensue, requiring ventilatory support.

Pulmonary function tests, including spirometry, measurement of lung volumes, and measurements of respiratory muscle strength, give important clues as to the cause and severity of the disease underlying the hypoventilation. In patients with neuromuscular disease, sleep-disordered breathing is evident when the FVC declines to <65% of predicted.[30] In patients with OHS, the restrictive pattern is accompanied by a decrease in the expiratory reserve volume.[31] Respiratory muscle strength is known to be decreased in patients with restrictive thoracic disorders, which correlates with the development of sleep-disordered breathing.[16] It is also decreased in patients with OHS due to a combination of abnormal respiratory mechanics and weak respiratory muscles.[32]

Because many of the disorders associated with the hypoventilation syndrome initially demonstrate more significant hypoxemia during sleep (particularly REM sleep) an overnight polysomnogram is often indicated. In addition, many disorders have associated obstructive and central sleep-disordered breathing events that would require appropriate treatment if recognized. A polysomnogram is indicated in patients with chest wall abnormalities and neuromuscular disease to identify patients who would benefit from nocturnal ventilation.[33] [34] [35] [36] [37] It identifies associated obstructive sleep apnea (OSA) in patients with OHS.[2] In addition, it may identify patients with OHS prior to developing awake elevations in $PaCO_2$.[38] In CHF with a left ventricular ejection fraction <45% and disturbed sleep, a polysomnogram identifies CSR.[5] [6] [7] [8] A polysomnogram is used in patients with COPD who have suspected overlap syndrome (associated OSA), but use to identify REM-associated hypoventilation is undefined.

An echocardiogram may be performed to evaluate for cor pulmonale and/or the presence of left-sided CHF. It documents the development of pulmonary hypertension in patients with OHS, neuromuscular disease, and COPD. In patients with CSR, an echocardiogram documents the severity of left ventricular dysfunction.[3][5] [6] [7] [8] [39]

A chest x-ray should be performed to exclude other causes for hypoxemia.

Other investigations

While an elevation of serum bicarbonate, as well as a low oxygen saturation on pulse oximetry, may suggest the presence of alveolar hypoventilation, they are not recommended as diagnostic tests. Measurement of serum bicarbonate may be used to screen for the presence of alveolar

hypoventilation, but does not confirm the diagnosis.[2] [40] Pulse oximetry suggests the presence of alveolar hypoventilation, but does not confirm the diagnosis and should not be used to decide when to measure $PaCO_2$.[40]

In the right clinical setting, other laboratory tests may be indicated. In patients with hypercapnia who demonstrate signs of hypothyroidism, measurement of thyroid-stimulating hormone levels may be indicated. Measurement of hematocrit is indicated in all patients with suspected or documented daytime and/or nocturnal hypoxemia. If there is a clinical suspicion for congenital central alveolar hypoventilation, mutations in the paired-like homeobox 2B (PHOX2B) gene should be evaluated, as mutations are noted in up to 91% of these patients.[24] Patients with PHOX2B mutations exhibit respiratory-related cortical activity on electroencephalograms at rest.[41]

History and exam

Other diagnostic factors

male sex (common)

- In patients with obesity hypoventilation syndrome, there is a 2:1 male-to-female ratio.[23]

dyspnea (common)

- Seen in most causes of hypoventilation syndrome.[16] [23] [28] As the syndrome progresses, dyspnea on exertion followed by dyspnea at rest is the most common symptom encountered by patients with hypoventilation.

daytime sleepiness (common)

- Can be seen with most causes of hypoventilation syndrome.[16] [23] [28] Daytime hypersomnolence resulting from nocturnal hypoventilation may progress and be associated with symptoms of morning headaches and fatigue.

morning headache (common)

- Can be seen with most causes of hypoventilation syndrome.[16] [23] [28]

impaired cough (common)

- Seen in patients with neuromuscular disease.[16] [28] Impaired cough in a disorder that causes respiratory muscle weakness may complicate the patient's course.

repeated lower respiratory tract infections (common)

- Seen in patients with neuromuscular disease.[16] [28] If a disorder causes respiratory muscle weakness, repeated lower respiratory tract infections may complicate the patient's course.

BMI ≥30 kg/m² (common)

- Seen in patients with obesity hypoventilation syndrome, which has an increasing prevalence with increasing BMI.[23]

increased pulmonic component of second heart sound (P2) (common)

- Can be seen with most causes of hypoventilation syndrome.[16] [23] [28]

lower-extremity edema (common)

- Can be seen with most causes of hypoventilation syndrome.[16] [23] [28]

right-sided third heart sound (S3 gallop) (common)

- Can be seen with most causes of hypoventilation syndrome.[16] [23] [28]

left-sided fourth heart sound (S4 gallop) (common)

- Can be seen in patients with Cheyne-Stokes respiration due to congestive heart failure.

Risk factors

Strong

body mass index (BMI) ≥30 kg/m²

- The prevalence of obesity hypoventilation syndrome in patients with obstructive sleep apnea significantly increases with increasing BMI.[23]

restrictive thoracic disorders

- Patients with chest wall deformities (kyphoscoliosis, fibrothorax, or thorocoplasty) and neuromuscular disorders, particularly Duchenne muscular dystrophy and other types of muscular dystrophies and spinal muscular atrophies, are at risk of hypoventilation.

central nervous system disorders

- Disorders include central sleep apnea syndromes, such as idiopathic central sleep apnea, and Cheyne-Stokes respiration. Another central but rare disorder is congenital central alveolar hypoventilation.[24]

obstructive airway disease

- Obstructive airway disease (in particular, COPD) can develop alveolar hypoventilation.

Investigations

1st test to order

Test	Result
arterial blood gas • Arterial blood gas is the definitive test used to confirm the diagnosis of alveolar hypoventilation and document the extent of associated hypoxemia.[29] [40]	**$PaCO_2$ >45 mmHg**
serum bicarbonate • May be used to screen for the presence of alveolar hypoventilation, but does not confirm the diagnosis.[2] [40]	**>24 mEq/L**
pulse oximetry • May be used to suggest the presence of alveolar hypoventilation, but does not confirm the diagnosis and should not be used to decide when to measure $PaCO_2$.[40]	**SaO_2 <90%**
hematocrit (Hct) • Indicated in all patients with suspected or documented daytime and/or nocturnal hypoxemia. • May be used to suggest the presence of alveolar hypoventilation, but is not routinely done.	**Hct >45%**

Other tests to consider

Test	Result
pulmonary function tests • In patients with neuromuscular disease, sleep-disordered breathing is evident when the FVC declines to <65% of predicted.[30] This is associated with the development of sleep-disordered breathing and alveolar hypoventilation.[42] In patients with obesity hypoventilation syndrome, the restrictive pattern is accompanied by a decrease in the expiratory reserve volume.[31]	**restrictive pattern on spirometry with reduced total lung capacity**
respiratory muscle strength • Known to be decreased in patients with restrictive thoracic disorders, which correlates with the development of sleep-disordered breathing.[16] Also decreased in patients with obesity hypoventilation syndrome due to a combination of abnormal respiratory mechanics and weak respiratory muscles.[32]	**decrease in maximal inspiratory and expiratory pressures**
CXR • Used to exclude other causes of hypoxemia. In patients with chest wall deformities such as kyphoscoliosis, a Cobb angle >120° (used to measure the spinal curvature) is associated with the development of nocturnal hypoventilation and the development of respiratory symptoms.[43]	**normal CXR in most cases; may show signs of congestive heart failure or lower respiratory tract infection if these complicate the condition**
polysomnogram • Indicated in patients with chest wall abnormalities and neuromuscular disease to identify patients who would benefit from nocturnal ventilation.[33] [34] [35] [36] [37] • Identifies associated obstructive sleep apnea (OSA) in patients with obesity hypoventilation syndrome (OHS).[2] In addition, it may identify patients with OHS prior to developing awake elevations in $PaCO_2$.[38] • In congestive heart failure with a left ventricular ejection fraction <45% and disturbed sleep, identifies Cheyne-Stokes respiration.[5] [6] [7] [8] • Used in patients with COPD who have suspected overlap syndrome (associated OSA), but use to identify REM-associated hypoventilation is undefined.	**demonstrates hypoventilation, particularly during REM sleep; may show obstructive or central apneas; sleep architecture is fragmented with an increase in arousals during the night**
echocardiogram • Documents the development of pulmonary hypertension in patients with obesity hypoventilation syndrome, neuromuscular disease, and COPD. In patients with Cheyne-Stokes respiration, documents the severity of left ventricular dysfunction.[3][5] [6] [7] [8] [39] • In patients with congestive heart failure and left ventricular ejection fraction <45%, Cheyne-Stokes respiration is reported in 33% to 42% of patients, with a prevalence as high as 56% in inpatients awaiting cardiac transplantation.[5] [6] [7] [8]	**demonstrates pulmonary hypertension (mean pulmonary artery pressure >25 mmHg)**
thyroid-stimulating hormone • Indicated in patients with hypercapnia who are suspected of having or who have symptoms/signs of hypothyroidism.	**elevated if primary hypothyroidism**
PHOX2B gene • If there is a clinical suspicion for congenital central alveolar hypoventilation, mutations in the paired-like homeobox 2B (PHOX2B) gene should be evaluated, as mutations are noted in up to 91% of	**heterozygous mutation**

Test	Result
these patients.[24] Suspected instances include newborns with signs of hypoventilation, or patients who present later in life with signs of hypoventilation following anesthesia or a pulmonary infection.[27]	

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Interstitial lung disease	• Patients with interstitial lung disease often complain of shortness of breath, especially exertional dyspnea. In addition, they may complain of a nonproductive cough. Patients can present with a rapid shallow breathing pattern, inspiratory crackles on examination of the lungs, and clubbing of the digits.	• While pulse oximetry may reveal an SaO_2 <90%, arterial blood gas analysis demonstrates hypocapnia rather than hypercapnia associated with hypoxemia. • CXR demonstrates interstitial changes and fibrosis, which can be confirmed with a CT scan.
Obstructive sleep apnea (OSA) without associated alveolar hypoventilation	• Patients with OSA without associated alveolar hypoventilation present with symptoms of excessive daytime sleepiness and loud snoring. On examination, obesity without signs of cor pulmonale such as lower-extremity edema is common, although one third of patients have a BMI <30 kg/m².	• Arterial blood gas analysis demonstrates a normal $PaCO_2$, and pulse oximetry while awake reveals a SaO_2 >90%. • Overnight polysomnogram shows obstructive apneas and hypopneas with nocturnal oxygen desaturation purely associated with the sleep-disordered breathing events.

Criteria

The American Academy of Sleep Medicine has published criteria for the diagnosis of sleep-related breathing disorders.[1] See also Central sleep apnea .

Obesity hypoventilation syndrome

- Hypoventilation is present during wakefulness ($PaCO_2$ ≥45 mmHg), as measured by arterial PCO_2, end-tidal PCO_2, or transcutaneous PCO_2. Sleep-related hypoventilation is inferred.
- Obesity is present (body mass index ≥30 kg/m²; ≥95th percentile for age and sex for children).
- Hypoventilation is not primarily due to lung parenchymal or airway disease, chest wall disorder (other than mass loading from obesity), medication use, neurologic disorder, muscle weakness, or a known congenital or idiopathic central alveolar hypoventilation syndrome.

Congenital central alveolar hypoventilation syndrome

- Sleep-related hypoventilation is present.
- Central nervous system autonomic dysfunction is present, usually due to a PHOX2B gene mutation.
- The disorder is not better explained by another sleep disorder, medical disorder, or medication/substance use.

Idiopathic central alveolar hypoventilation

- Sleep-related hypoventilation is present.
- Hypoventilation is not primarily due to lung parenchymal or airway disease, chest wall disorder, medication use, neurologic disorder, muscle weakness, obesity, or congenital hypoventilation syndromes.

Sleep-related hypoventilation due to a medical disorder

- Sleep-related hypoventilation is present.
- A lung parenchymal or airway disease, chest wall disorder, neurologic disorder, or muscle weakness is believed to be the primary cause of hypoventilation.
- Hypoventilation is not primarily due to obesity hypoventilation syndrome, medication use, or a known congenital central alveolar hypoventilation syndrome.

Screening

Patients with neuromuscular disease commonly develop sleep-disordered breathing, including alveolar hypoventilation, prior to the development of daytime hypercapnia, and sleep-disordered breathing is associated with disease progression.[42] Therefore, it is suggested that these patients be screened for the presence of sleep-disordered breathing at 6-month intervals to identify those who may benefit from therapeutic intervention.[44] [45]

When assessing people with suspected obstructive sleep apnea (OSA), commonly used screening questionnaires include the STOP-BANG (snoring, tiredness, observed apnea, blood pressure, body mass index, age, neck circumference, and sex) and the STOP (snoring, sleepiness, and other features associated with increased OSA risk such as obesity, increased neck girth, and hypertension). The Epworth Sleepiness Scale is a self-administered questionnaire in the preliminary assessment of sleepiness.[46] The higher the score, higher is the sleep propensity in daily life.[47] [48]

Testing includes pulmonary function tests, measurement of respiratory muscle strength, and assessment of central respiratory drive, which have been shown to predict the presence of sleep-disordered breathing in patients with primary myopathies.[16] [45] [49] Additional screening can include measurements of serum bicarbonate, hematocrit, and arterial blood gas. Polysomnograms are recommended to be done early in patients with myopathies and other restrictive disorders such as amyotrophic lateral sclerosis, due to the impact of therapy on quality of life and overall survival, which will be seen even before the development of daytime hypercapnia.[36] [44] [50] [51]

Approach

The primary treatment modality for the hypoventilation syndromes is nocturnal ventilation. With most disorders, nocturnal noninvasive ventilation (NIV) has become an increasingly used treatment option that is both effective and well tolerated.[29] Guidelines recommend appropriate titration techniques and methods for NIV in patients with the hypoventilation syndromes.[52] [53] With some disorders, especially with disease progression, invasive mechanical ventilation via tracheostomy may be indicated.

This topic focuses on obesity hypoventilation syndrome, restrictive thoracic disorders, Cheyne-Stokes respiration, and COPD.

See Central sleep apnea and Obstructive sleep apnea .

Obesity hypoventilation syndrome (OHS)

Continuous positive airway pressure (CPAP) may be used as an initial treatment of OHS, because most patients with OHS have associated obstructive sleep apnea.[40] There are reports of successful treatment of OHS with CPAP, usually requiring pressures of 12 to 14 cm H_2O.[13] [54] [55] [56] [57] [58] [59] [60] However, there are reports of failure with CPAP therapy as well when used alone.[54] [56] [61] [62] [63]

Bilevel positive airway pressure (PAP), with individually adjusted inspiratory and expiratory pressures, is probably the most effective noninvasive treatment for reversing the hypercapnia associated with OHS.[13] [64] [65] [66] With a pressure differential, bilevel PAP is more effective at ventilating than merely reversing upper airway obstruction as seen with CPAP. It should be considered during PAP titration when the oxygen saturation remains <90% despite the elimination of obstructive apneas and hypopneas.[52] Most studies have demonstrated that the differential between inspiratory PAP and expiratory PAP must be at least 8 to 10 cm H_2O to correct the hypercapnia and hypoxemia on a long-term basis with bilevel PAP therapy.[13] [67] [68] [69] [70] A retrospective study demonstrated good long-term outcome in patients treated with NIV after a mean follow-up of 4 years.[66] In addition, use of bilevel PAP results in better respiratory function improvement compared with CPAP.[70] In a prospective study, bilevel PAP was associated with greater PAP adherence when compared to CPAP therapy.[71] With either form of PAP therapy, patients who used their device for more than 6 hours had better improvement in arterial blood gases, improved quality of life scores, and a lower mortality compared to those that used their device for less than 6 hours.[71] It is now recommended that patients hospitalized with suspected OHS should be discharged on nocturnal NIV prior to having a formal outpatient titration study.[40]

Nocturnal invasive mechanical ventilation by tracheostomy can be used effectively in patients with severe OHS who have not been able to tolerate or have had unsuccessful treatment with noninvasive forms of PAP therapy.

Oxygen therapy should not be used alone in patients with OHS.[72] [73] However, approximately half of patients with OHS require the addition of oxygen to some form of PAP therapy.[13] [54] [74] [75] Oxygen therapy is added when bilevel has been titrated but there is residual oxygen desaturation in the absence of obstructive apneas and hypopneas.[52] Long-term use of PAP therapy often results in oxygen therapy no longer being required both nocturnally as well as during the day.[71]

Respiratory stimulants such as medroxyprogesterone have been used in reported cases of OHS, but they increase the risk of thromboembolic disease.[76] [77]

Weight reduction, including diet or the use of gastric bypass surgery, has been shown to be effective.[39] [40] Many of these patients with OHS require PAP therapy following surgery until they have lost a significant amount of weight. Even after significant weight loss, most gastric bypass surgery patients still have significant residual sleep-disordered breathing that requires continued use of NIV.[78]

Restrictive thoracic disorders

In patients with neuromuscular and chest wall diseases, the use of nocturnal ventilation has been associated with improved survival, sleep quality, daytime gas exchange, and daytime function and with decreased daytime sleepiness.[79] [80] [81] [82] In addition, improvements in respiratory muscle function are noted, which may explain the improvements in daytime gas exchange.[80] Overall, nocturnal ventilation can slow the rate of decline in pulmonary function compared with nonventilated controls.

Amyotrophic lateral sclerosis has become the most common restrictive thoracic disorder to be prescribed NIV, which reportedly improves survival and quality of life, and reduces decline in forced vital capacity.[51] [83] [84][85] Predictors of a favorable response to nocturnal NIV include intact bulbar function, orthopnea, hypercapnia, and nocturnal oxygen desaturation.[17] However, studies suggest that starting nocturnal NIV before the development of hypercapnia may be of benefit in patients with restrictive thoracic disorders.[44] [50] For patients with preserved bulbar function using NIV, mouthpiece ventilation may be suitable for daytime ventilatory support.[45]

NIV using either bilevel PAP or a volume-cycled ventilator is preferred, with the latter able to generate larger tidal volumes than the standard bilevel PAPs that have a maximum inspiratory PAP of 30 cm H_2O. Settings should be titrated in a sleep center or in a controlled setting such as the hospital, or, at times, in the patient's home. With PAP therapy, both inspiratory PAP and expiratory PAP should be increased together until all apneas and hypopneas are resolved, followed by continued increases in inspiratory PAP to correct the hypoxemia related to alveolar hypoventilation.[52]

Patients with neuromuscular diseases and hypoventilation may benefit from lung volume recruitment (LVR) (e.g., glossopharyngeal breathing or breath stacking using a handheld resuscitation bag or mouthpiece) and airway clearance (e.g., manually assisted cough techniques).[45]

Nocturnal invasive mechanical ventilation by tracheostomy often becomes necessary in patients intolerant of NIV, including those with extended daytime use, worsening bulbar function, frequent aspiration, insufficient cough, episodes of chest infection despite adequate secretion management, and declining lung function.[45] It may be necessary to add regular mechanical insufflation-exsufflation (cough assist device) for continued reduced cough effectiveness or high-frequency chest wall oscillation, with or without cough assistance or LVR, for patients with continued difficulties clearing secretions.[45]

Oxygen therapy should not be used alone in patients with hypoventilation syndrome due to restrictive thoracic disorders.

Cheyne-Stokes respiration

CPAP therapy has been shown to decrease the central apnea-hypopnea index in patients with Cheyne-Stokes respiration (CSR) due to congestive heart failure (CHF), both after short-term use and after periods of 1 to 3 months.[8] [86] [87] [88] [89] [90] [91] [92] By increasing intrathoracic pressure and decreasing the transmural pressure across the left ventricle, CPAP decreases left ventricular afterload, leading to an improvement in cardiac output.[13] It has been proposed that the increase in left ventricular ejection fraction with CPAP therapy reduces interstitial lung edema and decreases stimulation of the

pulmonary vagal afferents, which are thought to cause the observed hyperventilation and hypocapnia in these patients.[92] While a previous multicenter study did not reveal an improved transplant-free survival with CPAP, a post-hoc analysis of the data revealed an improved outcome in those patients assigned to CPAP therapy who were able to correct their apnea-hypopnea index to <15 events/hour after 3 months of use.[93] [94]

Bilevel PAP ventilation allows the individual adjustment of the inspiratory PAP and expiratory PAP and, when set with a backup rate, ensures ventilation during central apneic episodes. When compared with CPAP, both forms of therapy equally decreased the baseline apnea-hypopnea index and improved sleep quality and daytime fatigue.[87]

Adaptive servoventilation (ASV) is a form of noninvasive positive pressure ventilation that has been evaluated in the treatment of CSR. ASV provides a baseline degree of ventilatory support on top of an end-expiratory pressure of 5 cm H_2O and a default backup rate of 15 breaths/minute.[95] Inspiratory pressure increases from a low of 3 cm H_2O to a high of 10 cm H_2O to maintain ventilation at 90% of a running 3-minute reference period. When a decrease in ventilation is noted, such as during a central apnea, the inspiratory pressure increases to maintain ventilation, and then decreases again when spontaneous breathing resumes. Another device developed for ASV uses a flow-targeted approach to maintain ventilation. An end-expiratory pressure is adjusted to eliminate any obstructive events. The device then delivers an inspiratory PAP to maintain a target peak inspiratory airflow with a backup rate.[96] Comparing the one-night effects of CPAP, oxygen therapy, bilevel, and ASV, the apnea-hypopnea index decreased with all forms of therapy.[95] However, compared with baseline and the other treatments, ASV had the most significant improvement in the apnea-hypopnea index. The amount of slow-wave and REM sleep increased with ASV and was the preferred treatment modality. In a randomized study comparing ASV with CPAP, a more significant decrease in the apnea-hypopnea index was seen with ASV at both 3 and 6 months.[97] In addition, in a subset of patients who were evaluated, the left ventricular ejection fraction was noted to increase only in the ASV group at the end of 6 months. Overall, preliminary studies appeared to demonstrate that ASV was effective at normalizing the apnea-hypopnea index in patients with CSR. However, a large, end point-driven study demonstrated a higher all-cause mortality in patients receiving ASV compared with the control group. As a result, ASV is not recommended in patients with CHF and a LVEF ≤45% at this time until further analysis of the study is performed and the results from other ongoing trials are completed.[98] Using a flow-targeted ASV device, an ongoing trial has reported preliminary data showing increased hours of use each night and increased compliance at one year compared to those patients in the prior negative study.[99] In addition, there was no noted increase in mortality at one year in the patients treated with ASV. Final results and recommendations await the completion of this multicenter trial.

Nocturnal oxygen therapy has been shown to significantly decrease the apnea-hypopnea index, both acutely and after more prolonged therapy in patients with CSR due to CHF.[8][17] [58] [61] [62] [63] [100] [101] [102] [103] While oxygen therapy has been shown to decrease the apnea-hypopnea index, no study has demonstrated an improvement in left ventricular function in patients with CSR and CHF.[89] [100] [103]

Theophylline has been used for the treatment of CSR in CHF. Proposed mechanisms include improvement in cardiac function and thus circulation time, as well as a possible enhanced central respiratory drive effect.[104] [105] Acetazolamide induces a metabolic acidosis and thus increases minute ventilation. Studies have shown a decrease in the apnea-hypopnea index and number of arousals with acetazolamide.[106] [107] Both theophylline and acetazolamide have been described as being effective in

the treatment of CSR, but they are rarely used clinically. Practice parameters have been published to help guide physicians in regards to treatment options for CSR.[108]

COPD

The use of noninvasive positive pressure ventilation has been shown to be beneficial both during an acute exacerbation of COPD and in selected groups of patients with stable chronic emphysema.[109] [110] [111] [112] Nocturnal NIV has been shown to acutely improve sleep quality without an associated improvement in nocturnal gas exchange in a group of stable hypercapnic patients with COPD, suggesting that factors other than improvement in gas exchange, such as unloading inspiratory muscles or effects on central drive, might play a role.[110] Other long-term trials have demonstrated improvements in sleep quality and gas exchange and a decrease in hospital admissions and office visits.[111] [113] Nocturnal NIV combined with oxygen was shown to lower $PaCO_2$ and improve quality of life after two years in patients with hypercapnic COPD, when compared with oxygen therapy alone.[114] In addition, one trial noted improved survival in hypercapnic COPD patients who received NIV with oxygen therapy, compared with oxygen therapy alone.[112] One trial in patients with persistent hypercapnia following a recent COPD exacerbation, found that nocturnal NIV plus oxygen prolonged the time to readmission or death at 12 months when compared to just oxygen alone.[115] Guidelines have been developed for the use of noninvasive positive pressure ventilation in patients with stable COPD.[116]

The hypoxemia that develops in patients with alveolar hypoventilation most commonly is associated with hypercapnia. Thus, supplemental oxygen must be given with caution to these patients. In patients with COPD and hypoxemia, continuous low-flow oxygen has been shown to significantly affect mortality.[117] Yet, the use of nocturnal oxygen in COPD patients with REM-associated nocturnal oxygen desaturation has been shown to decrease pulmonary hypertension, but has no significant effect on mortality.[118]

Bilevel PAP can be initiated with most patients requiring an inspiratory PAP to expiratory PAP differential of at least 8 to 10 cm H_2O to have effective ventilation. Higher expiratory PAPs may be needed in those patients with the overlap syndrome where there is coexistent OSA. Otherwise, most patients may do well with an expiratory PAP of 5 cm H_2O, which is required to take up the dead space of the tubing and mask and allow effective sensing of an inspiratory effort. Excessive inspiratory PAPs are associated with increasing air leaks and less effective ventilation. However, pressure requirements vary greatly among patients.[119]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute		(summary)
obesity hypoventilation syndrome		
	1st	nocturnal ventilation
	plus	weight-reduction measures
	adjunct	nocturnal oxygen therapy
restrictive thoracic disorders		
	1st	nocturnal bilevel positive airway pressure or volume-cycled ventilation
	plus	lung volume recruitment + airway clearance techniques
	2nd	nocturnal invasive mechanical ventilation via tracheostomy
	plus	lung volume recruitment + airway clearance techniques
Cheyne-Stokes respiration		
	1st	nocturnal noninvasive ventilation + treatment of underlying disorder
	plus	nocturnal oxygen therapy
COPD		
	1st	nocturnal bilevel positive airway pressure + treatment of underlying disorder
	adjunct	nocturnal oxygen

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute

obesity hypoventilation syndrome

1st **nocturnal ventilation**

» Continuous positive airway pressure (CPAP) may be used as an initial treatment of obesity hypoventilation syndrome (OHS), because most patients with OHS have associated obstructive sleep apnea.[40] There are reports of successful treatment of OHS with CPAP, usually requiring pressures of 12 to 14 cm H_2O.[13] [54] [55] [56] [57] [58] [59] [60] However, there are reports of failure with CPAP therapy when used alone.[54] [56] [61] [62] [63]

» Bilevel positive airway pressure, with individually adjusted inspiratory positive airway pressure and expiratory positive airway pressure, is probably the most effective noninvasive treatment for reversing the hypercapnia associated with OHS.[13] [52] [64] [65] In addition, use of bilevel positive airway pressure results in better respiratory function improvement compared with CPAP and is associated with greater positive airway pressure adherence when compared to CPAP therapy.[70] [71]

» Most studies have demonstrated that the differential between inspiratory positive airway pressure and expiratory positive airway pressure must be at least 8 to 10 cm H_2O to correct the hypercapnia and hypoxemia on a long-term basis with bilevel positive airway pressure therapy.[13] [67] [68] [69] [70]

» Nocturnal invasive mechanical ventilation by tracheostomy can be used effectively in patients with severe obesity hypoventilation syndrome who have not been able to tolerate or have had unsuccessful treatment with noninvasive forms of positive airway pressure therapy.

plus **weight-reduction measures**

Treatment recommended for ALL patients in selected patient group

» Weight reduction, including diet or the use of gastric bypass surgery, has been shown to be effective.[39]

Acute

» Many of these patients with obesity hypoventilation syndrome require positive airway pressure therapy following surgery until they have lost a significant amount of weight.[78]

adjunct **nocturnal oxygen therapy**

Treatment recommended for SOME patients in selected patient group

» Oxygen therapy should not be used alone in patients with obesity hypoventilation syndrome (OHS).[72] [73] However, approximately half of patients with OHS require the addition of oxygen to some form of positive airway pressure therapy.[13] [54] [71][74] [75]

» Oxygen therapy is added when bilevel has been titrated but there is residual oxygen desaturation in the absence of obstructive apneas and hypopneas.[52]

restrictive thoracic disorders

1st **nocturnal bilevel positive airway pressure or volume-cycled ventilation**

» In patients with neuromuscular and chest wall diseases, the use of nocturnal ventilation has been associated with improved survival, sleep quality, daytime gas exchange, and daytime function and with decreased daytime sleepiness.[79] [80] [81] [82]

» Amyotrophic lateral sclerosis has become the most common restrictive thoracic disorder to be prescribed noninvasive ventilation (NIV), which reportedly improves survival and quality of life, and reduces decline in forced vital capacity.[83] [84] [85]

» NIV using either bilevel positive airway pressure or a volume-cycled ventilator is preferred, with the latter able to generate larger tidal volumes than the standard bilevel positive airway pressures that have a maximum inspiratory positive airway pressure of 30 cm H_2O. Settings should be titrated in a sleep center or in a controlled setting such as the hospital, or, at times, in the patient's home. With positive airway pressure therapy, both inspiratory positive airway pressure and expiratory positive airway pressure should be increased together until all apneas and hypopneas are resolved, followed by continued increases in inspiratory positive airway pressure to correct the hypoxemia related to alveolar hypoventilation.[52]

plus **lung volume recruitment + airway clearance techniques**

Acute

Treatment recommended for ALL patients in selected patient group

» Patients with neuromuscular diseases and hypoventilation may benefit from lung volume recruitment (LVR) (e.g., glossopharyngeal breathing or breath stacking using a handheld resuscitation bag or mouthpiece) and airway clearance (e.g., manually assisted cough techniques).[45]

» It may be necessary to add regular mechanical insufflation-exsufflation (cough assist device) for continued reduced cough effectiveness or high-frequency chest wall oscillation, with or without cough assistance or LVR, for patients with continued difficulties clearing secretions.[45]

2nd **nocturnal invasive mechanical ventilation via tracheostomy**

» Nocturnal invasive mechanical (NIV) ventilation by tracheostomy often becomes necessary in patients intolerant of NIV, including those with extended daytime use, worsening bulbar function, frequent aspiration, insufficient cough, episodes of chest infection despite adequate secretion management, and declining lung function.[45]

plus **lung volume recruitment + airway clearance techniques**

Treatment recommended for ALL patients in selected patient group

» Patients with neuromuscular diseases and hypoventilation may benefit from lung volume recruitment (LVR) (e.g., glossopharyngeal breathing or breath stacking using a handheld resuscitation bag or mouthpiece) and airway clearance (e.g., manually assisted cough techniques).[45]

» It may be necessary to add regular mechanical insufflation-exsufflation (cough assist device) for continued reduced cough effectiveness or high-frequency chest wall oscillation, with or without cough assistance or LVR, for patients with continued difficulties clearing secretions.[45]

Cheyne-Stokes respiration

1st **nocturnal noninvasive ventilation + treatment of underlying disorder**

» Continuous positive airway pressure (CPAP) therapy has been shown to decrease the central apnea-hypopnea index in patients with Cheyne-Stokes respiration (CSR) due to

Acute

congestive heart failure (CHF), both after short-term use and after periods of 1 to 3 months.[8] [86] [87] [88] [89] [90] [91] [92] By increasing intrathoracic pressure and decreasing the transmural pressure across the left ventricle, CPAP decreases left ventricular afterload, leading to an improvement in cardiac output.[13]

» Bilevel positive airway pressure ventilation allows the individual adjustment of the inspiratory positive airway pressure and expiratory positive airway pressure, and when set with a backup rate, ensures ventilation during central apneic episodes. When compared with CPAP, both forms of therapy equally decreased the baseline apnea-hypopnea index and improved sleep quality and daytime fatigue.[87]

» Another form of noninvasive positive pressure ventilation, referred to as adaptive servoventilation (ASV), has been evaluated in the treatment of CSR. ASV provides a baseline degree of ventilatory support on top of an end-expiratory pressure and a default backup rate.[95] [96] However, a large, end point-driven study demonstrated a higher all-cause mortality in patients receiving ASV compared with the control group. As a result, ASV is not recommended in patients with CHF and a left ventricular ejection fraction ≤45% at this time until further analysis of the study is performed and the results from other ongoing trials are completed.[98] Using a flow-targeted ASV device, an ongoing trial has reported preliminary data showing increased hours of use each night and increased compliance at one year as compared to those patients in the prior negative study.[99] In addition, there was no noted increase in mortality at one year in the patients treated with ASV. Final results and recommendations await the completion of this multicenter trial.

» Choice of methods is according to physician preference. Practice parameters have been published to help guide physicians in regards to treatment options for CSR.[108]

» Patients with CSR due to CHF should also receive treatment for CHF.

plus **nocturnal oxygen therapy**

Treatment recommended for ALL patients in selected patient group

» Nocturnal oxygen therapy has been shown to significantly decrease the apnea-hypopnea index, both acutely and after more prolonged

MANAGEMENT

Acute

therapy in patients with Cheyne-Stokes respiration (CSR) due to CHF.[8][17] [58] [61] [62] [63] [100] [101] [102][103]

» While oxygen therapy has been shown to decrease the apnea-hypopnea index, no study has demonstrated an improvement in left ventricular function in patients with CSR and CHF.[89][100][103]

COPD

1st **nocturnal bilevel positive airway pressure + treatment of underlying disorder**

» The use of noninvasive positive pressure ventilation has been shown to be beneficial both during an acute exacerbation of COPD and in selected groups of patients with stable chronic emphysema.[109] [110] [111] [112] [115] Nocturnal noninvasive ventilation has been shown to acutely improve sleep quality without an associated improvement in nocturnal gas exchange in a group of stable hypercapnic patients with COPD, suggesting that factors other than improvement in gas exchange, such as unloading inspiratory muscles or effects on central drive, might play a role.[110]

» Bilevel positive airway pressure can be initiated with most patients requiring an inspiratory positive airway pressure to expiratory positive airway pressure differential of at least 8 to 10 cm H_2O to have effective ventilation. Higher expiratory positive airway pressures may be needed in those patients with the overlap syndrome where there is coexistent obstructive sleep apnea. Otherwise, most patients may do well with an expiratory positive airway pressure of 5 cm H_2O, which is required to take up the dead space of the tubing and mask and allow effective sensing of an inspiratory effort. Excessive inspiratory positive airway pressures are associated with increasing air leaks and less effective ventilation. However, pressure requirements vary greatly among patients.[119]

» Patients should also receive treatment for COPD.

adjunct **nocturnal oxygen**

Treatment recommended for SOME patients in selected patient group

» The hypoxemia that develops in patients with alveolar hypoventilation most commonly is associated with hypercapnia. Thus, supplemental oxygen must be given with caution to these patients. In patients with COPD and

Acute

hypoxemia, continuous low-flow oxygen has been shown to significantly affect mortality.[117] Yet, the use of nocturnal oxygen in COPD patients with REM-associated nocturnal oxygen desaturation has been shown to decrease pulmonary hypertension, but has no significant effect on mortality.[118] Nocturnal noninvasive ventilation combined with oxygen was shown to lower $PaCO_2$ and improve quality of life after two years in hypercapnic COPD patients when compared with oxygen therapy alone, as well as demonstrating an improvement in survival.[112] [114][115]

Emerging

Average volume-assured pressure support (AVAPS)

AVAPS is a hybrid mode of ventilation that provides a more consistent tidal volume similar to volume-cycled ventilation, but with the comfort of pressure support ventilation.[65] In patients with obesity hypoventilation syndrome, AVAPS when compared with bilevel positive airway pressure was more effective at improving nocturnal transcutaneous CO_2 levels and arterial $PaCO_2$ at the end of 6 weeks.[65] However, sleep quality and quality of life were no different between the 2 modalities. In patients with COPD, AVAPS has been shown to decrease transcutaneous CO_2 levels more significantly compared with bilevel positive airway pressure, and was preferred by patients.[120]

Secondary prevention

Regular cleaning and replacement of parts or masks is important to prevent complications associated with the use of nocturnal ventilation (e.g., sinusitis, pneumonia). Patients with restrictive thoracic disorders may benefit from the use of a mechanical in-exsufflator to augment airflow during cough and allow secretion clearance to decrease the risk of complications such as pneumonia.[132]

Patient discussions

Patients who are receiving nocturnal ventilation should be instructed and trained on how to operate and care for their equipment. In many situations, especially in those requiring invasive ventilatory care with a tracheostomy, family members should also be trained on equipment operation and tracheostomy care. Patients should be educated on how to look for complications associated with the use of nocturnal ventilation, including signs and symptoms related to infection such as pneumonia or sinus infection.

In addition, patients should be instructed to avoid respiratory depressants, such as narcotics and sedatives, which could worsen their daytime symptoms and change their nocturnal ventilation requirements during sleep.

FOLLOW UP

Monitoring

Monitoring

Patients with underlying conditions associated with the hypoventilation syndromes are often monitored before treatment to identify signs and symptoms suggestive of alveolar hypoventilation, particularly during sleep. This is especially important in patients with underlying neuromuscular disease, where twice-yearly or yearly testing, including pulmonary function tests, arterial blood gas analysis, measurement of respiratory muscle strength, and overnight polysomnograms, may be indicated.[36] [37] In the same respect, many of these patients require similar testing after the start of ventilatory support, including with the use of nocturnal noninvasive ventilation, to ensure adequate treatment settings and to watch for disease progression.

Complications

Complications	Timeframe	Likelihood
cor pulmonale	**long term**	**medium**
As a result of diurnal CO_2 retention and associated hypoxemia, patients may demonstrate signs of cor pulmonale, including an increased P2, and lower-extremity edema.		
cardiac arrhythmia	**long term**	**medium**
Strong observational evidence implicates sleep-disordered breathing (e.g., obstructive and central sleep apnea, including Cheyne-Stokes breathing) in cardiac arrhythmogenesis (e.g., atrial fibrillation, ventricular tachyarrhythmias, sudden cardiac death, and bradyarrhythmias) by influencing the structural and electrophysiologic cardiac substrate.[121] Observational studies also suggest that effective treatment for sleep-disordered breathing reduces atrial fibrillation recurrence after rhythm control.[121]		
nasal congestion due to nocturnal noninvasive ventilation	**variable**	**medium**
As a result of using noninvasive ventilation with a nasal mask, patients can commonly develop a reactive nasal congestion. Heated humidification with the device is very helpful in treating or preventing nasal congestion, as is the use of intranasal corticosteroids and antihistamines.		
infections due to nocturnal noninvasive ventilation	**variable**	**medium**
Infections such as sinusitis can be seen with the use of a nasal mask for noninvasive ventilation. In addition, pneumonia can occasionally be related to the use of noninvasive ventilation, especially in those patients with neuromuscular disease and associated bulbar symptoms, where it is difficult to protect the airway.		
skin abrasions and breakdown due to nocturnal noninvasive ventilation	**variable**	**medium**
As a result of the use of nasal and nasal-oral masks, skin abrasions can develop. Patients can be fitted for a mask to attempt to decrease the risk of developing skin breakdown and to optimize comfort.		

Prognosis

The natural course for patients with disorders associated with hypoventilation syndromes varies depending on the underlying cause.

Observational data suggest an association between sleep-disordered breathing, especially obstructive sleep apnea (OSA), and increased risk for stroke, Alzheimer disease, Alzheimer disease-related dementias, Parkinson disease dementia, and all-cause dementia.[122] [123] [124] [125] [126] [127]

Obesity hypoventilation syndrome (OHS)

If left untreated, patients with mild OHS have a lower quality of life, increased somnolence, and more severe pulmonary hypertension compared with patients with OSA. Patients with OHS have a higher rate of ICU admission and need for mechanical ventilation than patients with similar degrees of obesity but without OHS.[128] One study demonstrated higher risk of postoperative respiratory failure and heart failure following elective noncardiac surgery in patients with OHS with OSA compared with patients with OSA alone.[129]

Appropriate early treatment of OHS is associated with reduced morbidity and mortality.[40][71][130]

Restrictive thoracic disorders

In many patients with hypoventilation syndrome due to neuromuscular disease, disease progression will eventually affect outcome. However, therapeutic interventions, such as nocturnal noninvasive ventilation, can have a significant effect on survival and quality of life.[50] [79] [80] [81] [84]

COPD

While disease severity will eventually predict outcome in patients with COPD, nocturnal noninvasive ventilation has been shown to improve gas exchange, sleep quality, and quality of life in these patients.[110] [111] [113] In addition, studies have noted improved survival in hypercapnic COPD patients who received noninvasive ventilation with oxygen therapy, compared with oxygen therapy alone.[112] [115]

Cheyne-Stokes respiration (CSR)

It has been demonstrated that in patients with congestive heart failure, mortality is higher in those with CSR than in those without CSR, despite a similar degree of heart failure.[131] While nocturnal noninvasive ventilation has been shown to improve heart function and significantly improve sleep-disordered breathing, its effect on transplant-free survival remains uncertain.[93] [94]

Diagnostic guidelines

International

International classification of sleep disorders. 3rd ed, text revision (https://aasm.org/clinical-resources/international-classification-sleep-disorders/) [1]

Published by: American Academy of Sleep Medicine **Last published:** 2023

Obstructive sleep apnea and cardiovascular disease: a scientific statement from the American Heart Association (https://professional.heart.org/en/guidelines-and-statements/guidelines-and-statements-search) [47]

Published by: American Heart Association **Last published:** 2021

Evaluation and management of obesity hypoventilation syndrome: an official American Thoracic Society clinical practice guideline (https://www.thoracic.org/statements) [40]

Published by: American Thoracic Society **Last published:** 2019

Congenital central hypoventilation syndrome: genetic basis, diagnosis and management: clinical policy statement (https://www.thoracic.org/statements/pediatric.php) [27]

Published by: American Thoracic Society **Last published:** 2010

ERS statement on respiratory muscle testing at rest and during exercise (https://channel.ersnet.org/channel-25-guidelines) [41]

Published by: European Respiratory Society **Last published:** 2019

Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s (https://www.nice.org.uk/guidance/ng202) [48]

Published by: National Institute for Health and Care Excellence (UK) **Last published:** 2021

Treatment guidelines

International

Respiratory management of patients with neuromuscular weakness: an American College of Chest Physicians clinical practice guideline and expert panel report (https://www.chestnet.org/Publications/CHEST-Publications/Guidelines-Consensus-Statements) [45]

Published by: American Heart Association **Last published:** 2023

Sleep disordered breathing and cardiac arrhythmias in adults: mechanistic insights and clinical implications: a scientific statement from the American Heart Association (https://professional.heart.org/en/guidelines-and-statements/guidelines-and-statements-search) [121]

Published by: American Heart Association **Last published:** 2022

Obstructive sleep apnea and cardiovascular disease: a scientific statement from the American Heart Association (https://professional.heart.org/en/guidelines-and-statements/guidelines-and-statements-search) [47]

Published by: American Heart Association **Last published:** 2021

Evaluation and management of obesity hypoventilation syndrome: an official American Thoracic Society clinical practice guideline (https://www.thoracic.org/statements) [40]

Published by: American Thoracic Society **Last published:** 2019

Home mechanical ventilation: a Canadian Thoracic Society clinical practice guideline (https://cts-sct.ca/guideline-library) [53]

Published by: Canadian Thoracic Society Home Mechanical Ventilation Committee **Last published:** 2011

Best clinical practices for the sleep center adjustment of noninvasive positive pressure ventilation (NPPV) in stable chronic alveolar hypoventilation syndromes (https://jcsm.aasm.org/toc/jcsm/06/05) [52]

Published by: NPPV Titration Task Force of the American Academy of Sleep Medicine **Last published:** 2010

Congenital central hypoventilation syndrome: genetic basis, diagnosis and management: clinical policy statement (http://www.thoracic.org/statements/pediatric.php) [27]

Published by: American Thoracic Society **Last published:** 2010

Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review) (http://www.aan.com/Guidelines/Home/ByTopic?topicId=19) [85]

Published by: American Academy of Neurology **Last published:** 2009 (reaffirmed 2023)

International

Clinical indications for noninvasive positive pressure ventilation in chronic respiratory failure due to restrictive lung disease, COPD, and nocturnal hypoventilation (https://journal.chestnet.org/issue/S0012-3692(15)X6174-5) [116]

Published by: Consensus Conference **Last published:** 1999

Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s (https://www.nice.org.uk/guidance/ng202) [48]

Published by: National Institute for Health and Care Excellence (UK) **Last published:** 2021

Key articles

- American Academy of Sleep Medicine. International classification of sleep disorders. 3rd ed, text revision. Darien, IL: American Academy of Sleep Medicine; 2023.
- Mokhlesi B, Masa JF, Brozek JL, et al. Evaluation and management of obesity hypoventilation syndrome. An official American Thoracic Society clinical practice guideline. Am J Respir Crit Care Med. 2019 Aug 1;200(3):e6-e24. Full text (https://www.atsjournals.org/doi/full/10.1164/rccm.201905-1071ST) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31368798?tool=bestpractice.bmj.com)
- Khan A, Frazer-Green L, Amin R, et al. Respiratory management of patients with neuromuscular weakness: an American College of Chest Physicians clinical practice guideline and expert panel report. Chest. 2023 Mar 13;S0012-3692(23)00353-7. Full text (https://erj.ersjournals.com/content/53/6/1801214.long) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/36921894?tool=bestpractice.bmj.com)
- National Institute for Health and Care Excellence. Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s. Aug 2021 [internet publication]. Full text (https://www.nice.org.uk/guidance/ng202)
- Miller RG, Jackson CE, Kasarskis EJ, et al; Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2009 Oct 13;73(15):1218-26. (Re-affirmed 2023.) Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2764727) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/19822872?tool=bestpractice.bmj.com)

References

1. American Academy of Sleep Medicine. International classification of sleep disorders. 3rd ed, text revision. Darien, IL: American Academy of Sleep Medicine; 2023.
2. Mokhlesi B, Tulaimat A, Faibussowitsch I, et al. Obesity hypoventilation syndrome: prevalence and predictors in patients with obstructive sleep apnea. Sleep Breath. 2007;11:117-124. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17187265?tool=bestpractice.bmj.com)
3. Kessler R, Chaouat A, Schinkewitch P, et al. The obesity-hypoventilation syndrome revisited: a prospective study of 34 consecutive cases. Chest. 2001;120:369-376. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1079891) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11502631?tool=bestpractice.bmj.com)
4. Lecube A, Sampol G, Lloberes P, et al. Asymptomatic sleep-disordered breathing in premenopausal women awaiting bariatric surgery. Obes Surg. 2010;20:454-461. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20020222?tool=bestpractice.bmj.com)

REFERENCES

5. Javaheri S, Parker TJ, Liming JD, et al. Sleep apnea in 81 ambulatory male patients with stable heart failure: types and their prevalences, consequences, and presentations. Circulation. 1998;97:2154-2159. Full text (http://circ.ahajournals.org/cgi/content/full/97/21/2154) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9626176?tool=bestpractice.bmj.com)

6. Sin DD, Fitzgerald F, Parker JD, et al. Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. Am J Respir Crit Care Med. 1999;160:1101-1106. Full text (http://www.atsjournals.org/doi/full/10.1164/ajrccm.160.4.9903020) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10508793?tool=bestpractice.bmj.com)

7. Oldenburg O, Lamp B, Faber L, et al. Sleep-disordered breathing in patients with symptomatic heart failure: a contemporary study of prevalence in and characteristics of 700 patients. Eur J Heart Fail. 2007;9:251-257. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17027333?tool=bestpractice.bmj.com)

8. Krachman SL, D'Alonzo GE, Berger TJ, et al. Comparison of oxygen therapy with nasal continuous positive airway pressure on Cheyne-Stokes respiration during sleep in congestive heart failure. Chest. 1999;116:1550-1557. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1078359) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10593775?tool=bestpractice.bmj.com)

9. Berthon-Jones M, Sullivan CE. Ventilatory and arousal responses to hypoxia in sleeping humans. Am Rev Respir Dis. 1982;125:632-639. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/6807150?tool=bestpractice.bmj.com)

10. Berthon-Jones M, Sullivan CE. Ventilation and arousal responses to hypercapnia in normal sleeping humans. J Appl Physiol. 1984;57:59-67. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/6432751?tool=bestpractice.bmj.com)

11. Berthon-Jones M, Sullivan CE. Time course of change in ventilatory response to CO2 with long-term CPAP therapy for obstructive sleep apnea. Am Rev Respir Dis. 1987;135:144-147. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/3099616?tool=bestpractice.bmj.com)

12. Zwillich CW, Sutton FD, Pierson DJ, et al. Decreased hypoxic ventilatory drive in the obesity-hypoventilation syndrome. Am J Med. 1975;59:343-348. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/1163544?tool=bestpractice.bmj.com)

13. Perez de Llano LA, Golpe R, Ortiz Piquer M, et al. Short-term and long-term effects of nasal intermittent positive pressure ventilation in patients with obesity-hypoventilation syndrome. Chest. 2005;128:587-594. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1083605) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16100142?tool=bestpractice.bmj.com)

14. Phipps PR, Starritt E, Caterson I, et al. Association of serum leptin with hypoventilation in human obesity. Thorax. 2002;57:75-76. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11809994?tool=bestpractice.bmj.com)

15. Piper AJ, Grunstein RR. Obesity hypoventilation syndrome: mechanisms and management. Am J Respir Crit Care Med. 2011;183:292-298. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/21037018?tool=bestpractice.bmj.com)

16. Ragette R, Mellies U, Schwake C, et al. Patterns and predictors of sleep disordered breathing in primary myopathies. Thorax. 2002;57:724-728. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12149535?tool=bestpractice.bmj.com)

17. Bourke SC, Bullock RE, Williams TL, et al. Noninvasive ventilation in ALS: indications and effect on quality of life. Neurology. 2003;61:171-177. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12874394?tool=bestpractice.bmj.com)

18. Naughton M, Benard D, Tam A, et al. Role of hyperventilation in the pathogenesis of central sleep apneas in patients with congestive heart failure. Am Rev Respir Dis. 1993;148:330-338. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/8342895?tool=bestpractice.bmj.com)

19. Hanly P, Zuberi N, Gray R. Pathogenesis of Cheyne-Stokes respiration in patients with congestive heart failure: relationship to arterial PCO2. Chest. 1993;104:1079-1084. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/8404170?tool=bestpractice.bmj.com)

20. Javaheri S. A mechanism of central sleep apnea in patients with heart failure. N Engl J Med. 1999;341:949-954. Full text (http://www.nejm.org/doi/full/10.1056/NEJM199909233411304#t=article) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10498490?tool=bestpractice.bmj.com)

21. Wilcox I, McNamara SG, Dodd MJ, et al. Ventilatory control in patients with sleep apnoea and left ventricular dysfunction: comparison of obstructive and central sleep apnoea. Eur Respir J. 1998;11:7-13. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9543263?tool=bestpractice.bmj.com)

22. Arzt M, Harth M, Luchner A, et al. Enhanced ventilatory response to exercise in patients with chronic heart failure and central sleep apnea. Circulation. 2003;107:1998-2003. Full text (http://circ.ahajournals.org/cgi/content/full/107/15/1998) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12695297?tool=bestpractice.bmj.com)

23. Mokhlesi B, Tulaimat A. Recent advances in obesity hypoventilation syndrome. Chest. 2007;132:1322-1336. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1085427) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17934118?tool=bestpractice.bmj.com)

24. Trang H, Dehan M, Beaufils F, et al; French CCHS Working Group. The French Congenital Central Hypoventilation Syndrome Registry: general data, phenotype, and genotype. Chest. 2005;127:72-79. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1083054) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15653965?tool=bestpractice.bmj.com)

25. Berry-Kravis EM, Zhou L, Rand CM, et al. Congenital central hypoventilation syndrome: PHOX2B mutations and phenotype. Am J Respir Crit Care Med. 2006;174:1139-1144. Full text (http://www.atsjournals.org/doi/full/10.1164/rccm.200602-305OC#.U1ZtQvldUww) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16888290?tool=bestpractice.bmj.com)

26. Doherty LS, Kiely JL, Deegan PC, et al. Late-onset central hypoventilation syndrome: a family genetic study. Eur Respir J. 2007;29:312-316. Full text (http://erj.ersjournals.com/content/29/2/312.full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17264323?tool=bestpractice.bmj.com)

27. Weese-Mayer DE, Berry-Kravis EM, Ceccherini I, et al. An official ATS clinical policy statement: congenital central hypoventilation syndrome: genetic basis, diagnosis and management. Am J

Respir Crit Care Med. 2010;181:626-644. Full text (http://www.atsjournals.org/doi/full/10.1164/rccm.200807-1069ST#.U1Ztf_ldUww) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20208042?tool=bestpractice.bmj.com)

28. Culebras A. Sleep disorders and neuromuscular disease. Semin Neurol. 2005;25:33-38. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15798935?tool=bestpractice.bmj.com)

29. Ozsancak A, D'Ambrosio C, Hill NS. Nocturnal noninvasive ventilation. Chest. 2008;133:1275-1286. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1085836) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18460530?tool=bestpractice.bmj.com)

30. Alves RS, Resende MB, Skomro RP, et al. Sleep and neuromuscular disorders in children. Sleep Med Rev. 2009;13:133-148. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18534877?tool=bestpractice.bmj.com)

31. Mokhlesi B, Kryger MH, Grunstein RR. Assessment and management of patients with obesity hypoventilation syndrome. Proc Am Thorac Soc. 2008;5:218-225. Full text (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2645254) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18250215?tool=bestpractice.bmj.com)

32. Koenig SM. Pulmonary complications of obesity. Am J Med Sci. 2001;321:249-279. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11307867?tool=bestpractice.bmj.com)

33. Sawicka EH, Branthwaite MA. Respiration during sleep in kyphoscoliosis. Thorax. 1987;42:801-808. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/3424256?tool=bestpractice.bmj.com)

34. Barthlen GM. Nocturnal respiratory failure as an indication of noninvasive ventilation in the patient with neuromuscular disease. Respiration. 1997;64(suppl 1):S35-S38. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9380959?tool=bestpractice.bmj.com)

35. Pradella M. Sleep polygraphic parameters in neuromuscular diseases. Arq Neuropsiquiatr. 1994;52:476-483. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/7611939?tool=bestpractice.bmj.com)

36. Bourke SC, Gibson GJ. Sleep and breathing in neuromuscular disease. Eur Respir J. 2002;19:1194-1201. Full text (http://erj.ersjournals.com/content/19/6/1194.full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12108875?tool=bestpractice.bmj.com)

37. Lofaso F, Quera-Salva MA. Polysomnography for the management of progressive neuromuscular disorders. Eur Respir J. 2002;19:989-990. Full text (http://erj.ersjournals.com/content/19/6/989.full.pdf+html) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12108883?tool=bestpractice.bmj.com)

38. Sivam S, Yee B, Wong K, et al. Obesity hypoventilation syndrome: early detection of nocturnal-only hypercapnia in an obese population. J Clin Sleep Med. 2018 Sep 15;14(9):1477-1484. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6134235) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30176974?tool=bestpractice.bmj.com)

39. Sugerman HJ, Fairman RP, Baron PL, et al. Gastric surgery for respiratory insufficiency of obesity. Chest. 1986;90:81-86. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/3720390?tool=bestpractice.bmj.com)

40. Mokhlesi B, Masa JF, Brozek JL, et al. Evaluation and management of obesity hypoventilation syndrome. An official American Thoracic Society clinical practice guideline. Am J Respir Crit Care Med. 2019 Aug 1;200(3):e6-e24. Full text (https://www.atsjournals.org/doi/full/10.1164/rccm.201905-1071ST) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31368798?tool=bestpractice.bmj.com)

41. Laveneziana P, Albuquerque A, Aliverti A, et al. ERS statement on respiratory muscle testing at rest and during exercise. Eur Respir J. 2019 Jun 13;53(6):1801214. Full text (https://erj.ersjournals.com/content/53/6/1801214.long) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30956204?tool=bestpractice.bmj.com)

42. Suresh S, Wales P, Dakin C, et al. Sleep-related breathing disorder in Duchenne muscular dystrophy: disease spectrum in the paediatric population. J Paediatr Child Health. 2005;41:500-503. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16150067?tool=bestpractice.bmj.com)

43. Ellis ER, Grunstein RR, Chan S, et al. Noninvasive ventilatory support during sleep improves respiratory failure in kyphoscoliosis. Chest. 1998;94:811-815. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/3139373?tool=bestpractice.bmj.com)

44. Ward S, Chatwin M, Heather S, et al. Randomized controlled trial on non-invasive ventilation (NIV) for nocturnal hypoventilation in neuromuscular and chest wall disease patients with daytime normocapnia. Thorax. 2005;60:1019-1024. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16299118?tool=bestpractice.bmj.com)

45. Khan A, Frazer-Green L, Amin R, et al. Respiratory management of patients with neuromuscular weakness: an American College of Chest Physicians clinical practice guideline and expert panel report. Chest. 2023 Mar 13;S0012-3692(23)00353-7. Full text (https://erj.ersjournals.com/content/53/6/1801214.long) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/36921894?tool=bestpractice.bmj.com)

46. Epworth Sleepiness Scale

47. Yeghiazarians Y, Jneid H, Tietjens JR, et al. Obstructive sleep apnea and cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2021 Jul 20;144(3):e56-67. Full text (https://www.ahajournals.org/doi/full/10.1161/CIR.0000000000000988) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/34148375?tool=bestpractice.bmj.com)

48. National Institute for Health and Care Excellence. Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s. Aug 2021 [internet publication]. Full text (https://www.nice.org.uk/guidance/ng202)

49. Weinberg J, Klefbeck B, Borg J, et al. Polysomnography in chronic neuromuscular disease. Respiration. 2003 Jul-Aug;70(4):349-54 Abstract (http://www.ncbi.nlm.nih.gov/pubmed/14512668?tool=bestpractice.bmj.com)

50. Lechtzin N, Scott Y, Busse AM, et al. Early use of non-invasive ventilation prolongs survival in subjects with ALS. Amyotroph Lateral Scler. 2007;8:185-188. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17538782?tool=bestpractice.bmj.com)

REFERENCES

51. Sancho J, Servera E, Bañuls P, et al. Prolonging survival in amyotrophic lateral sclerosis: efficacy of noninvasive ventilation and uncuffed tracheostomy tubes. Am J Phys Med Rehabil. 2010;89:407-411. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20407306?tool=bestpractice.bmj.com)

52. Berry RB, Chediak A, Brown LK, et al. Best clinical practices for the sleep center adjustment of noninvasive positive pressure ventilation (NPPV) in stable chronic alveolar hypoventilation syndromes. J Clin Sleep Med. 2010;6:491-509. Full text (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2952756/?tool=pubmed) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20957853?tool=bestpractice.bmj.com)

53. McKim DA, Road J, Avendano M, et al; Canadian Thoracic Society Home Mechanical Ventilation Committee. Home mechanical ventilation: a Canadian Thoracic Society clinical practice guideline. Can Respir J. 2011;18:197-215. Full text (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3205101) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22059178?tool=bestpractice.bmj.com)

54. Mokhlesi B, Tulaimat A, Evans AT, et al. Impact of adherence with positive airway pressure therapy on hypercapnia in obstructive sleep apnea. J Clin Sleep Med. 2006;2:57-62. Full text (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1894747) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17557438?tool=bestpractice.bmj.com)

55. Hida W, Okabe S, Tatsumi K, et al. Nasal continuous positive airway pressure improves quality of life in obesity hypoventilation syndrome. Sleep Breath. 2003;7:3-12. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12712392?tool=bestpractice.bmj.com)

56. Banerjee D, Yee, BJ, Piper AJ, et al. Obesity hypoventilation syndrome: hypoxemia during continuous positive airway pressure. Chest. 2007;131:1678-1684. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1085161) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17565018?tool=bestpractice.bmj.com)

57. Laaban JP, Orvoen-Frija E, Cassuto D, et al. Mechanisms of diurnal hypercapnia in sleep apnea syndromes associated with morbid obesity. Presse Med. 1996;25:12-16. (in French) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/8728885?tool=bestpractice.bmj.com)

58. Shivaram U, Cash ME, Beal A. Nasal continuous positive airway pressure in decompensated hypercapnic respiratory failure as a complication of sleep apnea. Chest. 1993;104:770-774. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/8365287?tool=bestpractice.bmj.com)

59. Piper AJ, Wang D, Yee BJ, et al. Randomised trial of CPAP vs bilevel support in the treatment of obesity hypoventilation syndrome without severe nocturnal desaturation. Thorax. 2008 May;63(5):395-401. Full text (http://thorax.bmj.com/content/63/5/395) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18203817?tool=bestpractice.bmj.com)

60. Howard ME, Piper AJ, Stevens B, et al. A randomised controlled trial of CPAP versus non-invasive ventilation for initial treatment of obesity hypoventilation syndrome. Thorax. 2017 May;72(5):437-444. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27852952?tool=bestpractice.bmj.com)

61. Laaban JP, Chailleux E. Daytime hypercapnia in adult patients with obstructive sleep apnea syndrome in France, before initiating nocturnal nasal continuous positive airway pressure therapy. Chest.

2005;127:710-715. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1083165) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15764748?tool=bestpractice.bmj.com)

62. Mokhlesi B. Positive airway pressure titration in obesity hypoventilation syndrome: continuous positive airway pressure or bilevel positive airway pressure. Chest. 2007;131:1624-1626. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1085173) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17565013?tool=bestpractice.bmj.com)

63. Schafer H, Ewig S, Hasper E, et al. Failure of CPAP therapy in obstructive sleep apnoea syndrome: predictive factors and treatment with bilevel-positive airway pressure. Respir Med. 1998;92:208-215. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9616514?tool=bestpractice.bmj.com)

64. Budweiser S, Riedl SG, Jorres RA, et al. Mortality and prognostic factors in patients with obesity-hypoventilation syndrome undergoing noninvasive ventilation. J Intern Med. 2007;261:375-383. Full text (http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2796.2007.01765.x/full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17391112?tool=bestpractice.bmj.com)

65. Storre JH, Seuthe B, Fiechter R, et al. Average volume-assured pressure support in obesity hypoventilation: a randomized crossover trial. Chest. 2006;130:815-821. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1084691) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16963680?tool=bestpractice.bmj.com)

66. Priou P, Hamel JF, Person C, et al. Long-term outcome of noninvasive positive pressure ventilation for obesity hypoventilation syndrome. Chest. 2010;138:84-90. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/20348200?tool=bestpractice.bmj.com)

67. Berger KI, Ayappa I, Chatr-Amontri B, et al. Obesity hypoventilation syndrome as a spectrum of respiratory disturbances during sleep. Chest. 2001;120:1231-1238. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1080061) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11591566?tool=bestpractice.bmj.com)

68. Redolfi S, Corda L, La Piana G, et al. Long-term non-invasive ventilation increases chemosensitivity and leptin in obesity-hypoventilation syndrome. Respir Med. 2007;101:1191-1195. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17189682?tool=bestpractice.bmj.com)

69. de Lucas-Ramos P, de Miguel-Diez J, Santacruz-Siminiani A, et al. Benefits at 1 year of nocturnal intermittent positive pressure ventilation in patients with obesity-hypoventilation syndrome. Respir Med. 2004;98:961-967. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15481272?tool=bestpractice.bmj.com)

70. Masa JF, Corral J, Alonso ML, et al. Efficacy of different treatment alternatives for obesity hypoventilation syndrome. Am J Respir Crit Care Med. 2015;192:86-95. Full text (https://www.atsjournals.org/doi/10.1164/rccm.201410-1900OC) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25915102?tool=bestpractice.bmj.com)

71. Bouloukaki I, Mermigkis C, Michelakis S, et al. The association between adherence to positive airway pressure therapy and long-term outcomes in patients with obesity hypoventilation syndrome: a prospective observational study. J Clin Sleep Med. 2018 Sep 15;14(9):1539-1550. Full text

(http://jcsm.aasm.org/ViewAbstract.aspx?pid=31380) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30176976?tool=bestpractice.bmj.com)

72. Masa JF, Celli BR, Riesco JA, et al. Noninvasive positive pressure ventilation and not oxygen may prevent overt ventilatory failure in patients with chest wall diseases. Chest. 1997 Jul;112(1):207-13. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9228378?tool=bestpractice.bmj.com)

73. Hollier CA, Harmer AR, Maxwell LJ, et al. Moderate concentrations of supplemental oxygen worsen hypercapnia in obesity hypoventilation syndrome: a randomised crossover study. Thorax. 2014 Apr;69(4):346-53. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/24253834?tool=bestpractice.bmj.com)

74. Masa JF, Celli BR, Riesco JA, et al. The obesity hypoventilation syndrome can be treated with noninvasive mechanical ventilation. Chest. 2001;119:1102-1107. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11296176?tool=bestpractice.bmj.com)

75. Heinemann F, Budweiser S, Dobroschke J, et al. Non-invasive positive pressure ventilation improves lung volumes in the obesity hypoventilation syndrome. Respir Med. 2007;101:1229-1235. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17166707?tool=bestpractice.bmj.com)

76. Poulter NR, Chang CL, Farley TM, et al. Risk of cardiovascular diseases associated with oral progestagen preparations with therapeutic indications. Lancet. 1999;354:1610. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10560679?tool=bestpractice.bmj.com)

77. Kimura H, Tatsumi K, Kunitomo F, et al. Obese patients with sleep apnea syndrome treated by progesterone. Tohoku J Exp Med. 1988;156:151-157. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/2479120?tool=bestpractice.bmj.com)

78. Lettieri CJ, Eliasson AH, Greenburg DL. Persistence of obstructive sleep apnea after surgical weight loss. J Clin Sleep Med 2008;4:333-338. Full text (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2542489) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/18763424?tool=bestpractice.bmj.com)

79. Young HK, Lowe A, Fitzgerald DA, et al. Outcome of noninvasive ventilation in children with neuromuscular disease. Neurology. 2007;68:198-201. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17224573?tool=bestpractice.bmj.com)

80. Piper AJ, Sullivan CE. Effects of long-term nocturnal nasal ventilation on spontaneous breathing during sleep in neuromuscular and chest wall disorders. Eur Respir J. 1996;9:1515-1522. Full text (http://erj.ersjournals.com/content/9/7/1515.full.pdf+html) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/8836668?tool=bestpractice.bmj.com)

81. Mellies U, Ragette R, Dohna Schwake CD, et al. Longterm noninvasive ventilation in children and adolescents with neuromuscular disorders. Eur Respir J. 2003;22:631-636. Full text (http://erj.ersjournals.com/content/22/4/631.full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/14582916?tool=bestpractice.bmj.com)

82. Annane D, Orlikowski D, Chevret S. Nocturnal mechanical ventilation for chronic hypoventilation in patients with neuromuscular and chest wall disorders. Cochrane Database Syst Rev. 2014;

(12):CD001941. Full text (http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001941.pub3/full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25503955?tool=bestpractice.bmj.com)

83. Laub M, Midgren B. Survival of patients on home mechanical ventilation: a nationwide prospective study. Respir Med. 2007;101:1074-1078. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17118638?tool=bestpractice.bmj.com)

84. Bourke SC, Tomlinson M, Williams TL, et al. Effects of non-invasive ventilation on survival and quality of life in patients with amyotrophic lateral sclerosis: a randomised controlled trial. Lancet Neurol. 2006;5:140-147. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16426990?tool=bestpractice.bmj.com)

85. Miller RG, Jackson CE, Kasarskis EJ, et al; Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2009 Oct 13;73(15):1218-26. (Re-affirmed 2023.) Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2764727) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/19822872?tool=bestpractice.bmj.com)

86. Takasaki Y, Orr D, Popkin J, et al. Effect of nasal continuous positive airway pressure on sleep apnea in congestive heart failure. Am Rev Respir Dis. 1989;140:1578-1584. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/2690705?tool=bestpractice.bmj.com)

87. Kohnlein T, Welte T, Tan LB, et al. Assisted ventilation for heart failure patient with Cheyne-Stokes respiration. Eur Respir J. 2002;20:934-941. Full text (http://erj.ersjournals.com/content/20/4/934.full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12412686?tool=bestpractice.bmj.com)

88. Naughton MT, Liu PP, Benard DC, et al. Treatment of congestive heart failure and Cheyne-Stokes respiration during sleep by continuous positive airway pressure. Am J Respir Crit Care Med. 1995;151:92-97. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/7812579?tool=bestpractice.bmj.com)

89. Arzt M, Schulz M, Wensel R, et al. Nocturnal continuous positive airway pressure improves ventilatory efficiency during exercise in patients with chronic heart failure. Chest. 2005;127:794-802. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1083207) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15764759?tool=bestpractice.bmj.com)

90. Naughton MT, Benard DC, Liu PP, et al. Effects of nasal CPAP on sympathetic activity in patients with heart failure and central sleep apnea. Am J Respir Crit Care Med. 1995;152:473-479. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/7633695?tool=bestpractice.bmj.com)

91. Walsh JT, Andrews R, Starling R, et al. Effects of captopril and oxygen on sleep apnoea in patients with mild to moderate congestive cardiac failure. Br Heart J. 1995;73:237-241. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/7727183?tool=bestpractice.bmj.com)

92. Naughton MT, Benard DC, Rutherford R, et al. Effect of continuous positive airway pressure on central sleep apnea and nocturnal PCO2 in heart failure. Am J Respir Crit Care Med. 1994;150:1598-1604. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/7952621?tool=bestpractice.bmj.com)

93. Bradley TD, Logan AG, Kimoff RJ, et al. Continuous positive airway pressure for central sleep apnea and heart failure. N Engl J Med. 2005;353:2025-2033. Full text (http://www.nejm.org/doi/

full/10.1056/NEJMoa051001#t=article) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16282177?tool=bestpractice.bmj.com)

94. Arzt M, Floras JS, Logan AG, et al. Suppression of central sleep apnea by continuous positive airway pressure and transplant-free survival in heart failure. Circulation. 2007 Jun 26;115(25):3173-80. Full text (http://circ.ahajournals.org/content/115/25/3173.full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17562959?tool=bestpractice.bmj.com)

95. Teschler H, Döhring J, Wang YM, et al. Adaptive pressure support servo-ventilation: a novel treatment for Cheyne-Stokes respiration in heart failure. Am J Respir Crit Care Med. 2001;164:614-619. Full text (http://www.atsjournals.org/doi/full/10.1164/ajrccm.164.4.9908114) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/11520725?tool=bestpractice.bmj.com)

96. Arzt M, Wensel R, Montalvan S, et al. Effects of dynamic bilevel positive airway pressure support on central sleep apnea in men with heart failure. Chest. 2008;134:61-66. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1085946) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17951617?tool=bestpractice.bmj.com)

97. Pepperell JC, Maskell NA, Jones DR, et al. A randomized controlled trial of adaptive ventilation for Cheyne-Stokes breathing in heart failure. Am J Respir Crit Care Med. 2003;168:1109-1114. Full text (http://www.atsjournals.org/doi/full/10.1164/rccm.200212-1476OC) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12928310?tool=bestpractice.bmj.com)

98. Cowie MR, Woehrle H, Wegscheider K, et al. Adaptive servo-ventilation for central sleep apnea in systolic heart failure. N Engl J Med. 2015;373:1095-105. Full text (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4779593) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/26323938?tool=bestpractice.bmj.com)

99. Perger E, Lyons OD, Inami T, et al. Predictors of 1-year compliance with adaptive servoventilation in patients with heart failure and sleep disordered breathing: preliminary data from the ADVENT-HF trial. Eur Respir J. 2019 Feb 21;53(2). Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30409822?tool=bestpractice.bmj.com)

100. Hanly PJ, Millar TW, Steljes DG, et al. The effect of oxygen on respiration and sleep in patients with congestive heart failure. Ann Intern Med. 1989;111:777-782. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/2817624?tool=bestpractice.bmj.com)

101. Franklin KA, Eriksson P, Sahlin C, et al. Reversal of central sleep apnea with oxygen. Chest. 1997 Jan;111(1):163-9. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/8996011?tool=bestpractice.bmj.com)

102. Lorenzi-Filho G, Rankin F, Bies I, et al. Effects of inhaled carbon dioxide and oxygen on Cheyne-Stokes respiration in patients with heart failure. Am J Respir Crit Care Med. 1999;159:1490-1498. Full text (http://www.atsjournals.org/doi/pdf/10.1164/ajrccm.159.5.9810040) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10228116?tool=bestpractice.bmj.com)

103. Krachman SK, Nugent T, Crocetti J, et al. Effects of oxygen therapy on left ventricular function in patients with Cheyne-Stokes respiration and congestive heart failure. J Clin Sleep Med. 2005;1:271-276. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17566188?tool=bestpractice.bmj.com)

104. Sanders JS, Berman TM, Barlett MM, et al. Increased hypoxic ventilatory drive due to administration of aminophylline in normal men. Chest. 1980;78:279-282. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/6772387?tool=bestpractice.bmj.com)

105. Javaheri S, Parker TJ, Wexler L, et al. Effect of theophylline on sleep-disordered breathing in heart failure. N Engl J Med. 1996;335:562-567. Full text (http://www.nejm.org/doi/full/10.1056/NEJM199608223350805#t=article) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/8678934?tool=bestpractice.bmj.com)

106. DeBacker WA, Verbraecken J, Willemen M, et al. Central apnea index decreases after prolonged treatment with acetazolamide. Am J Respir Crit Care Med. 1995;151:87-91. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/7812578?tool=bestpractice.bmj.com)

107. Javaheri S. Acetazolamide improves central sleep apnea in heart failure: a double-blind, prospective study. Am J Respir Crit Care Med. 2006;173:234-237. Full text (http://www.atsjournals.org/doi/full/10.1164/rccm.200507-1035OC#.U1Zwm_ldUww) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16239622?tool=bestpractice.bmj.com)

108. Aurora RN, Chowdhuri S, Ramar K, et al. The treatment of central sleep apnea syndromes in adults: practice parameters with an evidence-based literature review and meta-analyses. Sleep. 2012;35:17-40. Full text (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3242685) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/22215916?tool=bestpractice.bmj.com)

109. Antonelli M, Conti G, Rocco M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med. 1998;339:429-435. Full text (http://www.nejm.org/doi/full/10.1056/NEJM199808133390703#t=article) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9700176?tool=bestpractice.bmj.com)

110. Krachman SL, Quaranta AJ, Berger TJ, et al. Effects of noninvasive positive pressure ventilation on gas exchange and sleep in COPD patients. Chest. 1997 Sep;112(3):623-8. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9315793?tool=bestpractice.bmj.com)

111. Jones SE, Packham S, Hebden M, et al. Domiciliary nocturnal intermittent positive pressure ventilation in patients with respiratory failure due to severe COPD: long-term follow-up and effect on survival. Thorax. 1998:53:495-498. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/9713450?tool=bestpractice.bmj.com)

112. McEvoy RD, Pierce JR, Hillman PD, et al. Nocturnal non-invasive nasal ventilation in stable hypercapnic COPD: a randomised controlled trial. Thorax. 2009;64:561-566. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/19213769?tool=bestpractice.bmj.com)

113. Elliott MW, Simonds AK, Carroll MP, et al. Domiciliary nocturnal nasal intermittent positive pressure ventilation in hypercapnic respiratory failure due to chronic obstructive lung disease: effects on sleep and quality of life. Thorax. 1992;47:342-348. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/1609376?tool=bestpractice.bmj.com)

114. Clini E, Sturani C, Rossi A, et al. The Italian multicentre study on noninvasive ventilation in chronic obstructive pulmonary disease patients. Eur Respir J. 2002;20:529-538. Full text (http://

erj.ersjournals.com/content/20/3/529.full) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/12358325?tool=bestpractice.bmj.com)

115. Murphy PB, Rehal S, Arbane G, et al. Effect of home noninvasive ventilation with oxygen therapy vs oxygen therapy alone on hospital readmission or death after an acute COPD exacerbation: a randomized clinical trial. JAMA. 2017 Jun 6;317(21):2177-2186. Full text (https://jamanetwork.com/journals/jama/fullarticle/2627985) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/28528348?tool=bestpractice.bmj.com)

116. Anon. Clinical indications for noninvasive positive pressure ventilation in chronic respiratory failure due to restrictive lung disease, COPD, and nocturnal hypoventilation: a consensus conference report. Chest. 1999;116:521-534. Full text (http://journal.publications.chestnet.org/article.aspx?articleid=1078113) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10453883?tool=bestpractice.bmj.com)

117. Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial. Ann Intern Med. 1980;93:391-398. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/6776858?tool=bestpractice.bmj.com)

118. Chaouat A, Weitzenblum E, Kessler R, et al. A randomized trial of nocturnal oxygen therapy in chronic obstructive pulmonary disease patients. Eur Respir J. 1999;14:1002-1008. Full text (http://erj.ersjournals.com/content/14/5/1002.full.pdf+html) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/10596681?tool=bestpractice.bmj.com)

119. Tuggey JM, Elliott MW. Titration of non-invasive positive pressure ventilation in chronic respiratory failure. Respir Med. 2006;100:1262-1269. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/16310352?tool=bestpractice.bmj.com)

120. Ekkernkamp E, Storre JH, Windisch W, et al. Impact of intelligent volume-assured pressure support on sleep quality in stable hypercapnic chronic obstructive pulmonary disease patients: a randomized, crossover study. Respiration. 2014;88:270-276. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25171686?tool=bestpractice.bmj.com)

121. Mehra R, Chung MK, Olshansky B, et al. Sleep-disordered breathing and cardiac arrhythmias in adults: mechanistic insights and clinical implications: a scientific statement from the American Heart Association. Circulation. 2022 Aug 30;146(9):e119-e136. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10227720) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/35912643?tool=bestpractice.bmj.com)

122. Gottesman RF, Lutsey PL, Benveniste H, et al. Impact of sleep disorders and disturbed sleep on brain health: a scientific statement from the American Heart Association. Stroke. 2024 Mar;55(3):e61-76. Full text (https://www.ahajournals.org/doi/full/10.1161/STR.0000000000000453) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/38235581?tool=bestpractice.bmj.com)

123. Titova OE, Yuan S, Baron JA, et al. Sleep-disordered breathing-related symptoms and risk of stroke: cohort study and Mendelian randomization analysis. J Neurol. 2022 May;269(5):2460-8. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9021054) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/34596745?tool=bestpractice.bmj.com)

124. Xie C, Zhu R, Tian Y, et al. Association of obstructive sleep apnoea with the risk of vascular outcomes and all-cause mortality: a meta-analysis. BMJ Open. 2017 Dec 22;7(12):e013983. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5770910) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/29275335?tool=bestpractice.bmj.com)

125. Dong JY, Zhang YH, Qin LQ. Obstructive sleep apnea and cardiovascular risk: meta-analysis of prospective cohort studies. Atherosclerosis. 2013 Aug;229(2):489-95. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23684511?tool=bestpractice.bmj.com)

126. Tsai MS, Li HY, Huang CG, et al. Risk of alzheimer's disease in obstructive sleep apnea patients with or without treatment: real-world evidence. Laryngoscope. 2020 Sep;130(9):2292-8. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/32045010?tool=bestpractice.bmj.com)

127. Guay-Gagnon M, Vat S, Forget MF, et al. Sleep apnea and the risk of dementia: a systematic review and meta-analysis. J Sleep Res. 2022 Oct;31(5):e13589. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/35366021?tool=bestpractice.bmj.com)

128. Nowbar S, Burkart KM, Gonzales R, et al. Obesity-associated hypoventilation in hospitalized patients: prevalence, effects, and outcome. Am J Med. 2004;116:1-7. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/14706658?tool=bestpractice.bmj.com)

129. Kaw R, Bhateja P, Mar HP, et al. Postoperative complications in patients with unrecognized obesity hypoventilation syndrome undergoing elective noncardiac surgery. Chest. 2016;149:84-91. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/25996642?tool=bestpractice.bmj.com)

130. Kreivi HR, Itäluoma T, Bachour A. Effect of ventilation therapy on mortality rate among obesity hypoventilation syndrome and obstructive sleep apnoea patients. ERJ Open Res. 2020 May 11;6(2):00101-2019. Full text (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7211948) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/32420312?tool=bestpractice.bmj.com)

131. Hanly PJ, Zuberi-Khokhar NS. Increased mortality associated with Cheyne-Stokes respiration in patients with congestive heart failure. Am J Respir Crit Care Med. 1996;153:272-6. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/8542128?tool=bestpractice.bmj.com)

132. Miske LJ, Hickey EM, Kolb SM, et al. Use of the mechanical in-exsufflator in pediatric patients with neuromuscular disease and impaired cough. Chest. 2004 Apr;125(4):1406-12. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/15078753?tool=bestpractice.bmj.com)

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This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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